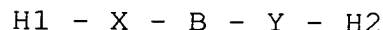

AN IN VIVO SCREEN USING CHEMICAL INDUCERS OF DIMERIZATION

Abstract of the Disclosure

The subject invention provides a compound having the formula:

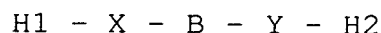


B¹
wherein each of H1 and H2 may be the same or different and capable of binding to a receptor which is the same or different; wherein each of X and Y may be present or absent and if present, each may be the same or different spacer moiety; and wherein B is an enzyme cleavable moiety. In an embodiment, H1 can be methotrexate. This invention also provides a method of screening proteins for the ability to catalyze bond cleavage, and for the ability to catalyze bond formation.

AN IN VIVO SCREEN USING CHEMICAL INDUCERS OF DIMERIZATION

Abstract of the Invention

The subject invention provides a compound having the formula:



wherein each of H1 and H2 may be the same or different and capable of binding to a receptor which is the same or different; wherein each of X and Y may be present or absent and if present, each may be the same or different spacer moiety; and wherein B is an enzyme cleavable moiety. In an embodiment, H1 can be methotrexate. This invention also provides a method of screening proteins for the ability to catalyze bond cleavage, and for the ability to catalyze bond formation. ~~comprising the steps of:~~

~~—— a) providing a cell that expresses a pair of fusion proteins which upon dimerization change a cellular readout;~~

~~—— b) providing the compound of the invention which dimerizes the pair of fusion proteins, said compound comprising two portions coupled by a bond that is cleavable by the protein to be screened; and~~

~~—— c) screening for the cellular readout, wherein a change the cellular readout indicates catalysis of bond cleavage by the protein to be screened. Finally, the invention also provides a method of screening proteins for the ability to catalyze bond formation, comprising the steps of:~~

~~—— a) providing a cell that expresses a pair of fusion proteins which upon dimerization activate a cellular readout;~~

~~—— b) providing a first compound and a second compound, each being capable of binding to one of the pair of fusion proteins, said first and second compound comprising a portion through which the first and second compounds are coupled to form the inventive compound by the action of the bond forming protein to be screened; and~~

~~—— c) screening for the cellular readout, wherein a change in the cellular readout indicates catalysis of bond formation by the protein to be screened.~~